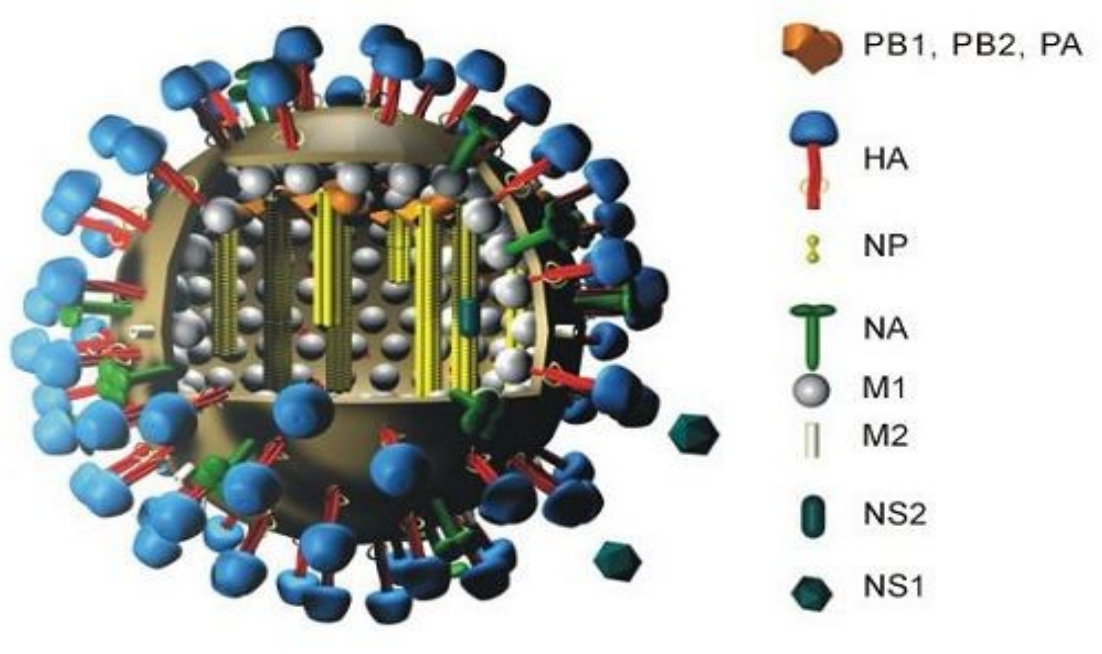
MOLECULAR VIROLOGY



Fedik Abdul Rantam, DVM, Dr, Prof.
VIROLOGY AND IMMUNOLOGY
DEP OF MICROBIOLOGY, VET MED. AU

MOLECULAR VIROLOGY

Virus are:

- Organisme subseluler with life cycle as parasite in the cell
- Without metabolism activity out of cell
- Consist genetic materials RNA or DNA

MOLECULAR VIROLOGY

- Consist some molecular to form virus particle
- Molecular like Nucleotide, amino acid, peptide, protein, enzyme
- Needed : transcription, translation, assembling, virus release, epitope
- To build: structural protein and nonstructural

VIRUS COMPARTMENT

- Nucleic acid around protein consist more lipid and sugar
- Virion function to transfer of genome in to the cell for replication
- Receptor or effectors specific for attachtment and transfer into the cell
- Protein is important role as molecule of virus to design of their pathogenesis

Bahan Dasar Virus

- Protein : structural protein and non structural protein consist nucleoprotein, capsid protein, envelop protein and enzyme
- Amino acid: genetic code to protein synthesis and production as new virus (progeny)

PROTEIN PRODUCE OF SINGLE GEN

- mRNA splicing
- Read through of stop codon
- Multiple star sites
- Overlapping genes
- Polyprotein cleavage
- Ribosomal frame shifting

mRNA Splicing

- Protein produce through sequent mechanism of part of intron in precursor, who near with exon to ligate again Example : Parvovirus, adenovirus, herpesvirus (latent infection of herpes virus)

Readthrough of Stop Codons

- Protein produce of viral gene through mechanism of reading stop codon, who tRNA molecule to inside as amino acid no more correlation with polypeptide chain Example: retrovirus

Multiple Start Sites

- Protein produce of gene viral through build new genetic material in some places
- Example Herpes virus, hepadna virus, papova virus, adeno virus

Overlapping Genes

- Protein viral synthesis through mechanism of single nucleotide sequence from single strand with the function as two protein, but needed two open reading frames. Example *AUG*GCAA*AUG*GGCCUUUUACACAA (AUG:MET)
- Example: hepadna virus, papova virus

Polyprotein Cleavage

- Protein viral synthesis through cleavage gene mechanism after translation
- Example: Picorna virus

Ribosomal Framshifting

- Protein viral gene synthesis through build framshifting between upstream and down stream
- Example : Retro virus

Definition

- Swine Flu viral is taken from name of influenza cases which caused by Orthomyxo virus which be endemic in swine population.
- Isolate of Swine flu were classified by one of the subtype virus from influenza A genus

PANDEMIC OF INFLUENZA

1918 - 1919 "SPANISH FLU"
A (H1N1)

virus origin from
avian waterfowl

STILL CIRCULATE TODAY

1957 - 1958 "ASIAN FLU"
A (H2N2)

HA, NA, PB1 = Avian

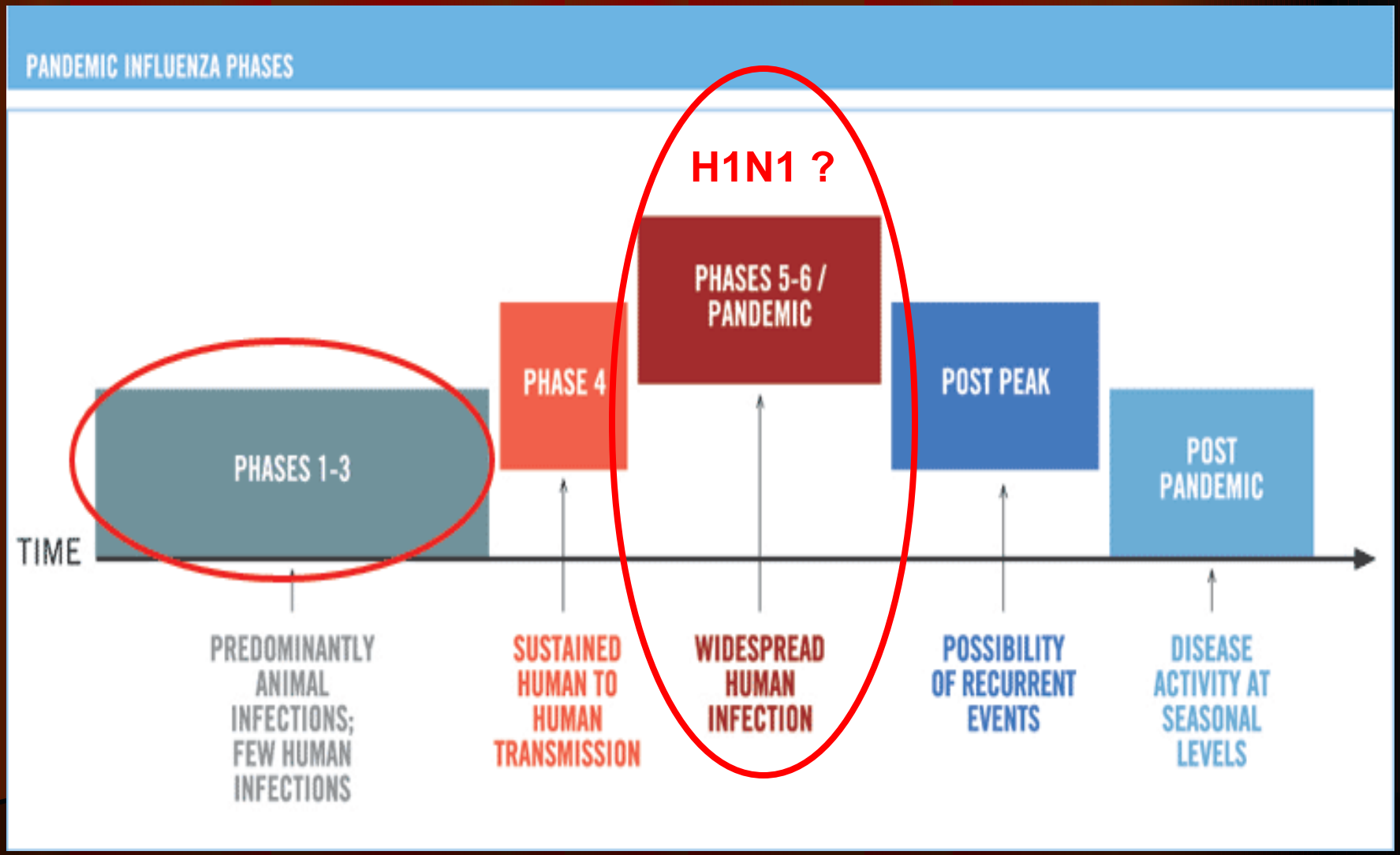
Virus have gen combination
from human dr virus influenza
& avian waterfowl virus
influenza and swine

1968 - 1969 "HONG KONG FLU"
A (H3N2)

HA, PB1 = Avian

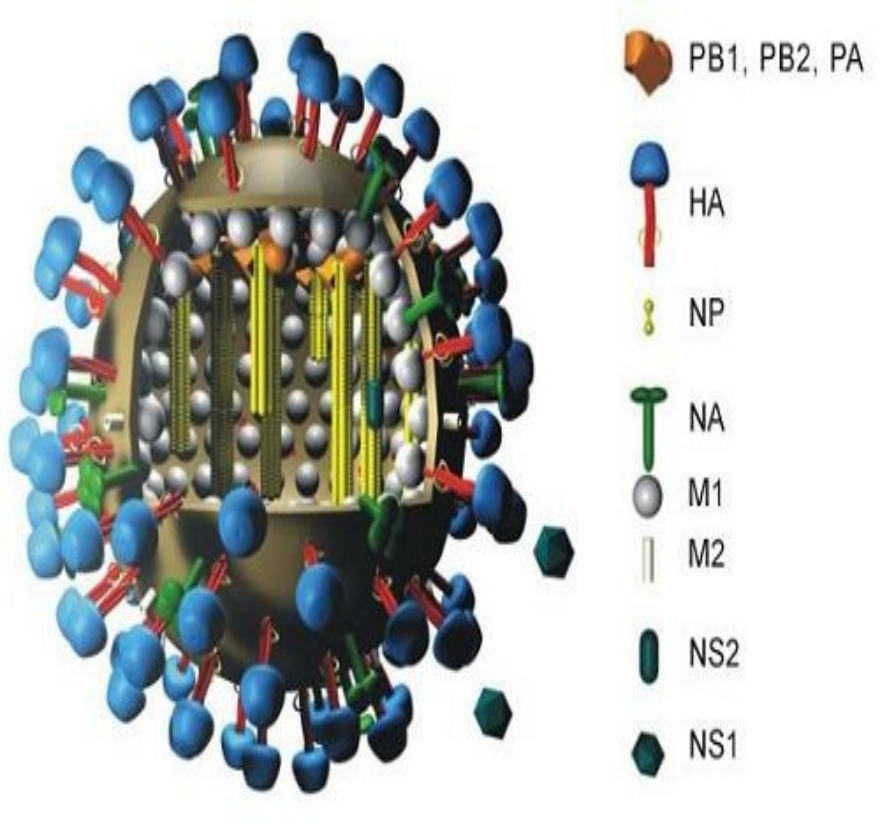
Pandemic
H1N1 ?
HA, NA

PANDEMIC PHASE OF INFLUENZA (WHO)

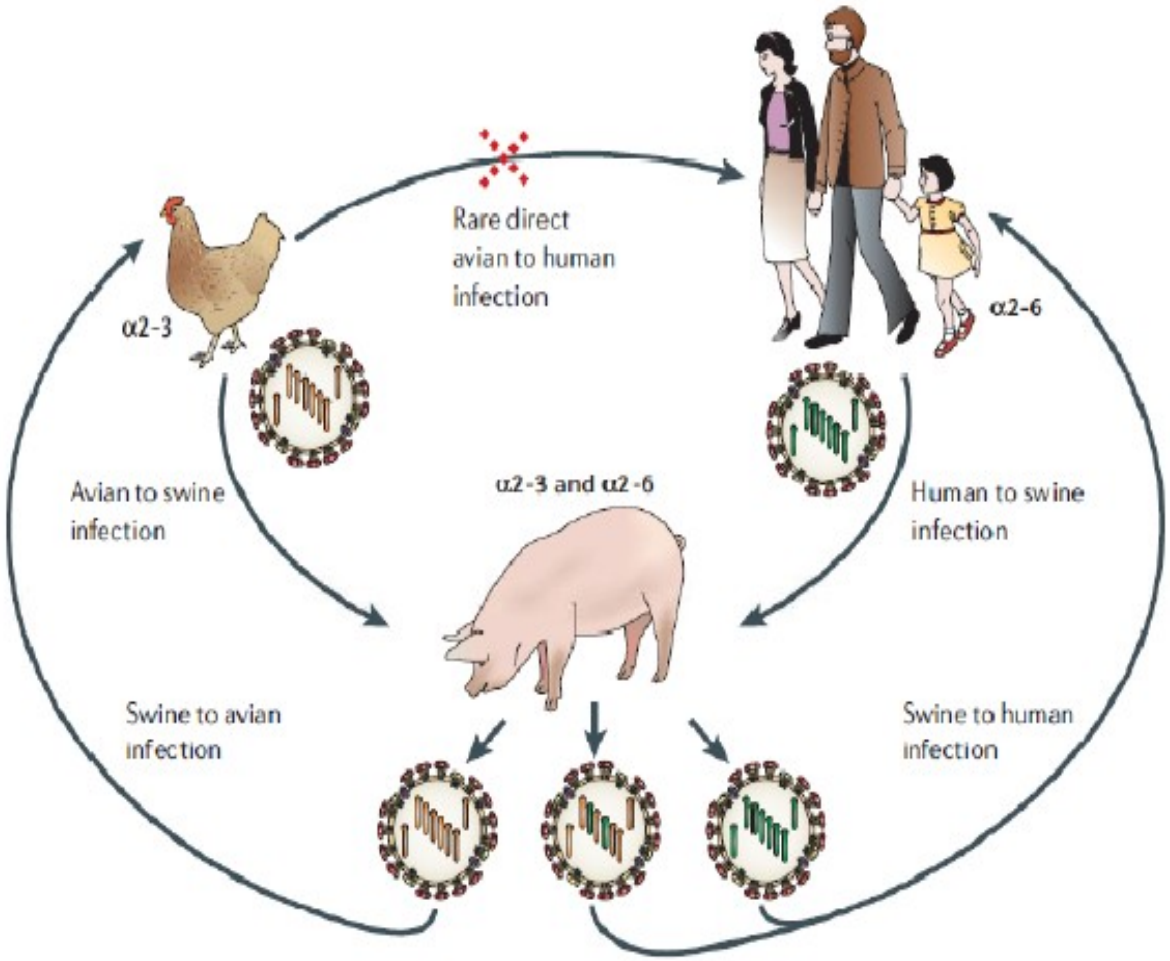


CHARACTERISTIC OF SWINE INFLUENZA VIRUS

- Type: A, B, C
- Diameter 80 - 120 nm
- Pleomorphic, spherical, filamentous particles
- Single-stranded RNA
- Segmented genome, 8 segments in A and B
- Hemagglutinin and Neuraminidase on surface of virion

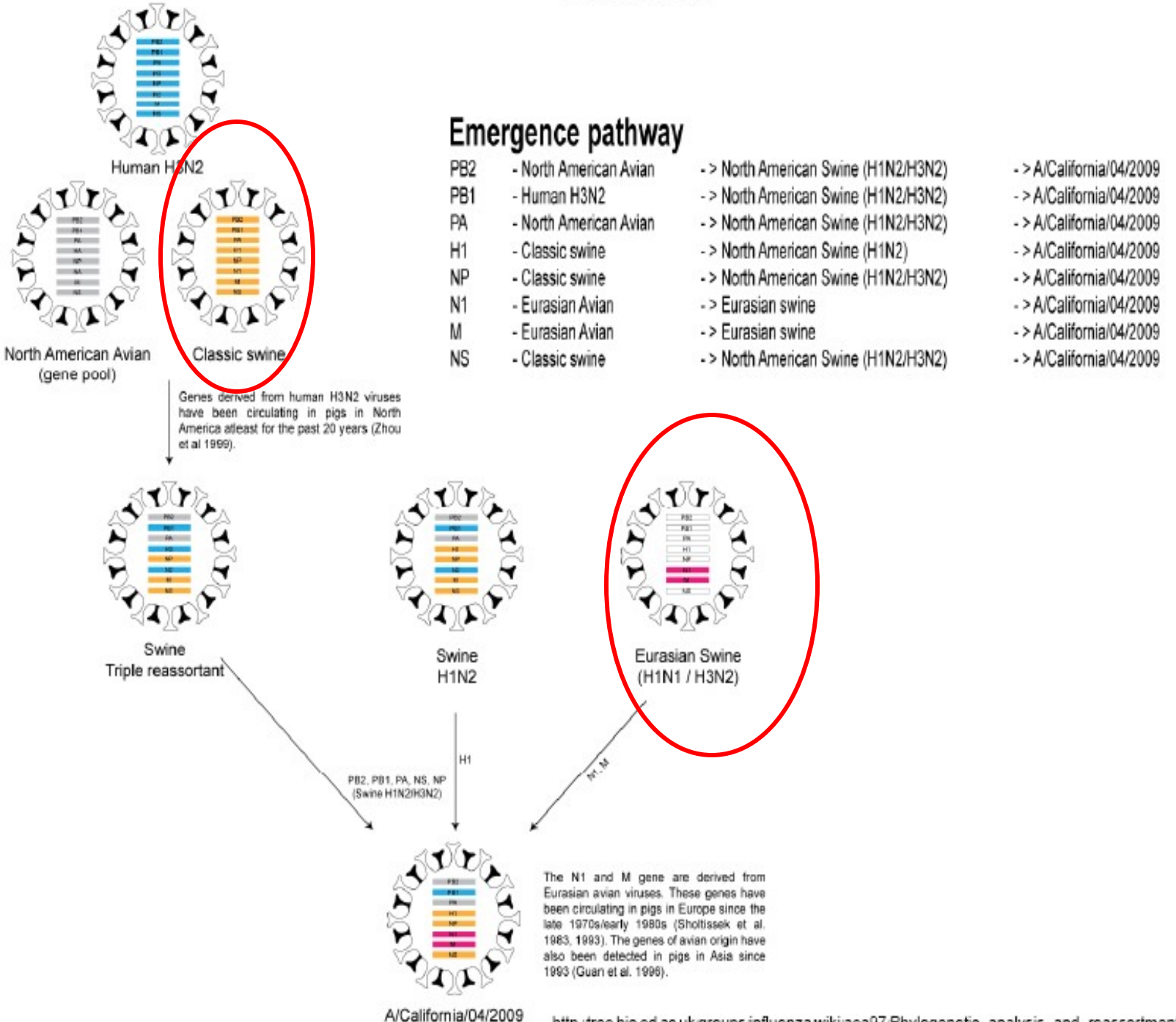


Mechanisms for the emergence of pandemic influenza A virus strain



Information Genetik Changing

- Its happen if: Increasing of segment RNA count, so this condition cause of *low fidelity* and mutation/ genetic variation.This condition was called with *antigenic drift*, if new genetic variant was arise, so its be different with old genetic, and this condition is called with *antigenic shift*.

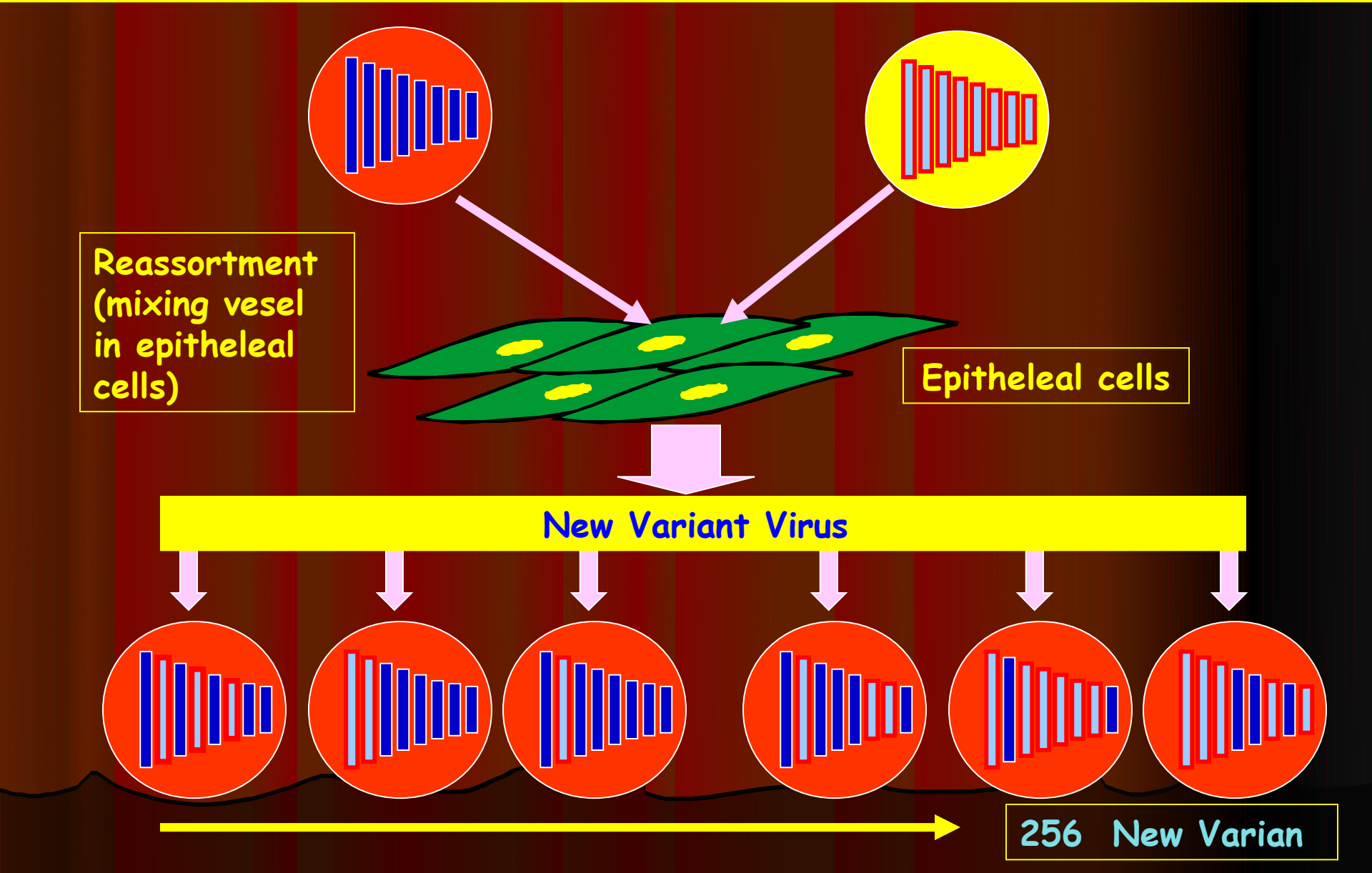


Emergence pathway

PB2	- North American Avian	-> North American Swine (H1N2/H3N2)	-> A/California/04/2009
PB1	- Human H3N2	-> North American Swine (H1N2/H3N2)	-> A/California/04/2009
PA	- North American Avian	-> North American Swine (H1N2/H3N2)	-> A/California/04/2009
H1	- Classic swine	-> North American Swine (H1N2)	-> A/California/04/2009
NP	- Classic swine	-> North American Swine (H1N2/H3N2)	-> A/California/04/2009
N1	- Eurasian Avian	-> Eurasian swine	-> A/California/04/2009
M	- Eurasian Avian	-> Eurasian swine	-> A/California/04/2009
NS	- Classic swine	-> North American Swine (H1N2/H3N2)	-> A/California/04/2009

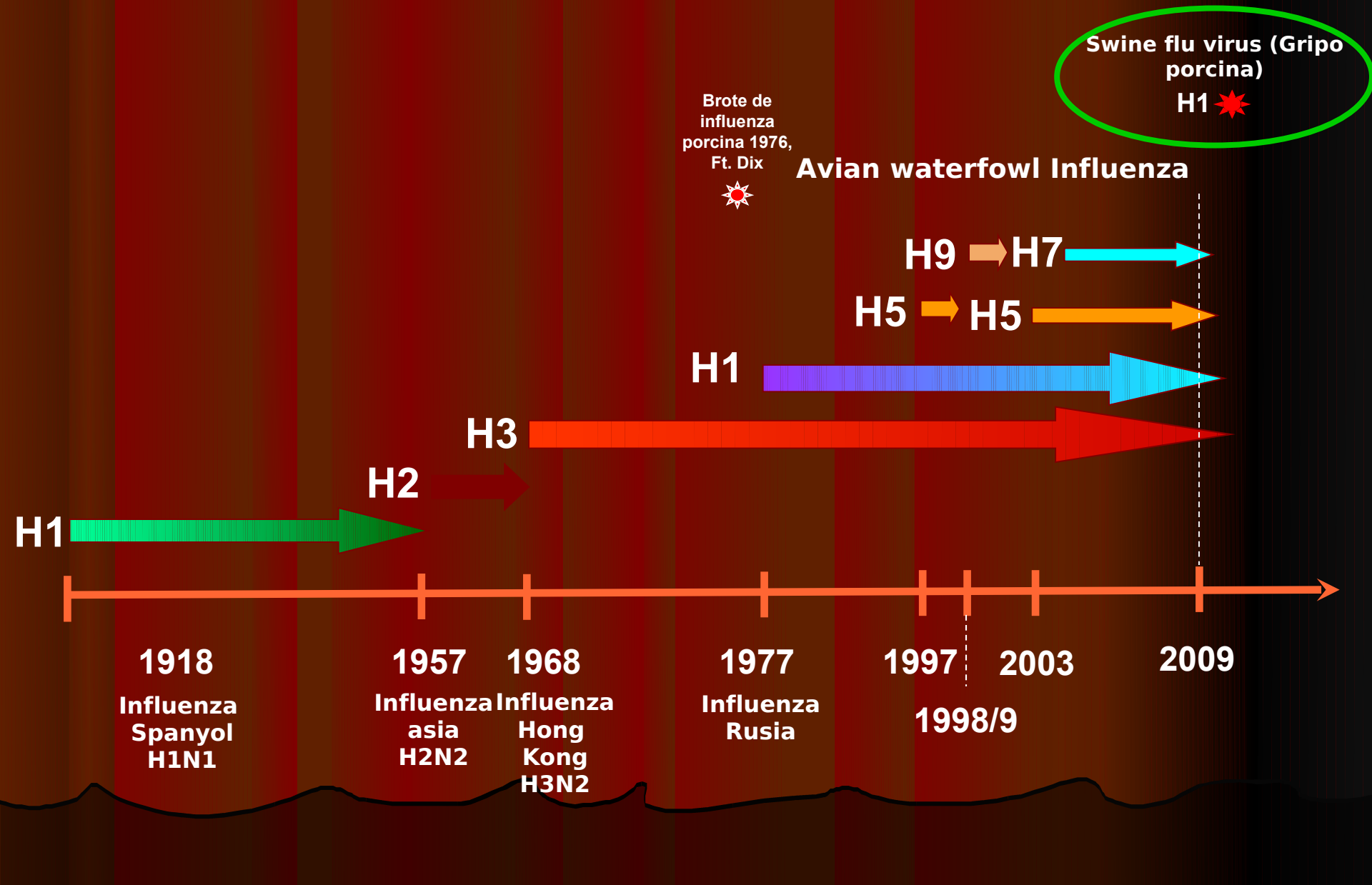
http://tree.bio.ed.ac.uk/groups/influenza/wiki/aea97/Phylogenetic_analysis_and_reassortment.html

SEGMEN GENOM INFLUENZA VIRUS CHANGING IN *MIX INFECTION*



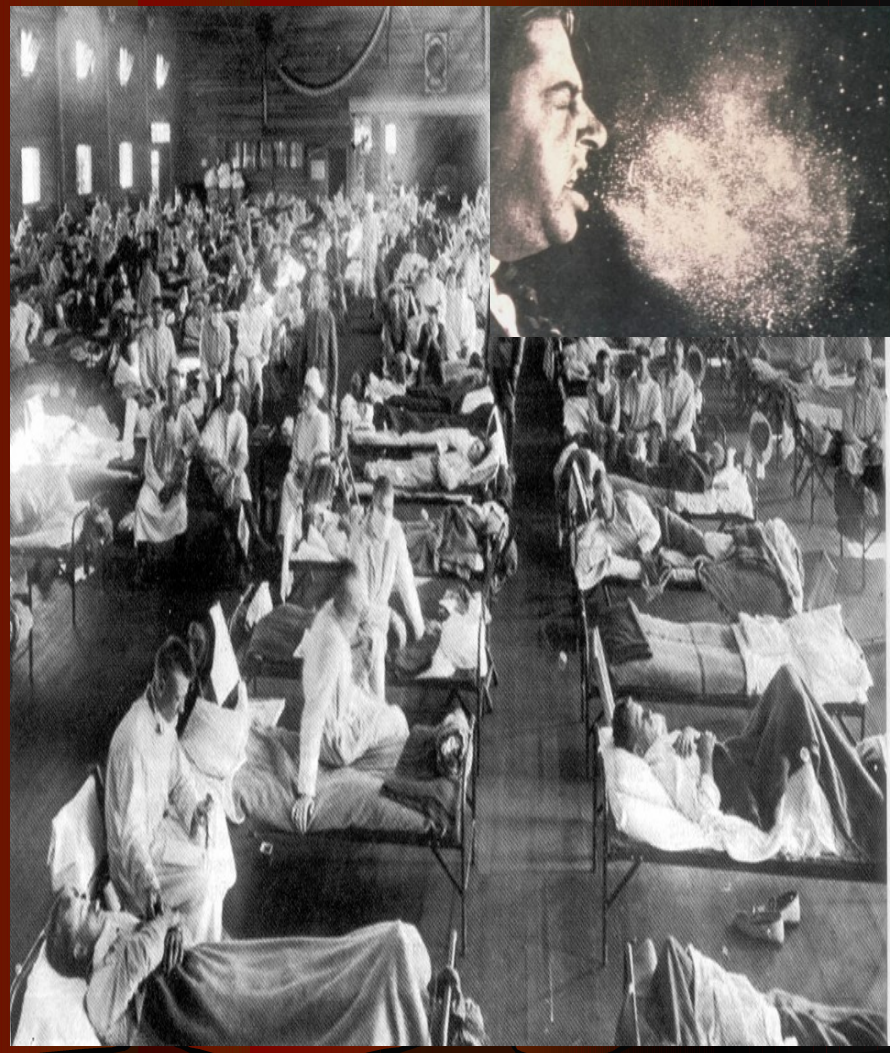
CRONOLOGIS OF EMERGING DISEASE

(Swine Flu)



EMERGENCY OF INFLUENZA

- Agent, that are necessary global attention
- Influenza virus is causing epidemy around at 1500’an, and pandemy is knowing around at 1889.
- Pandemic accident at 1918 to1919, that caused people dead around 20 million.

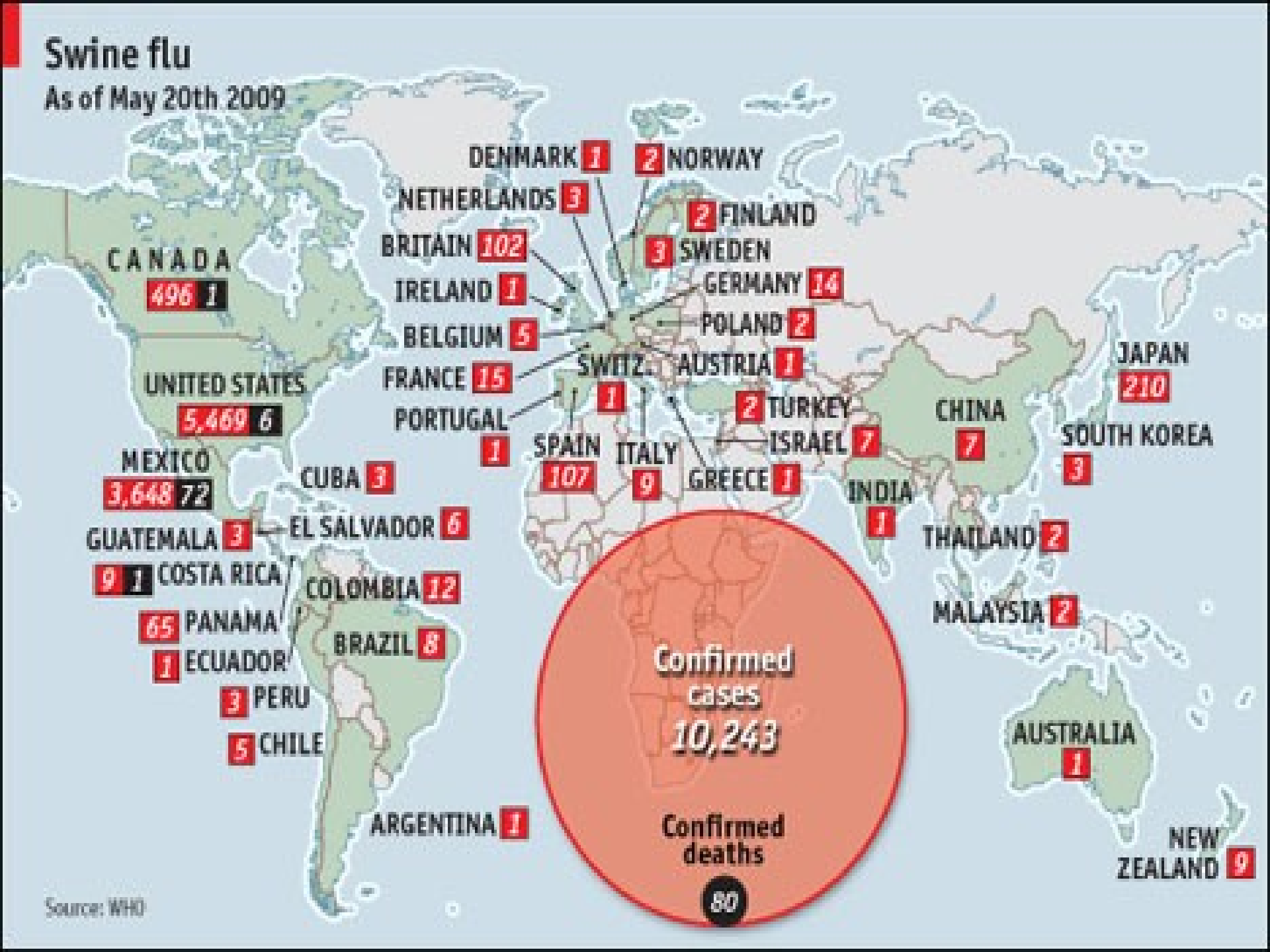


SWINE FLU DIFFERENT WITH HUMAN FLU

- H1N1 influenza A virus or Swine flu antigenicaly difference with H1N1 influenza A virus on human.
- No more protective if seasonal vaccine of influenza was using for preventive of H1N1 influenza A virus infection.

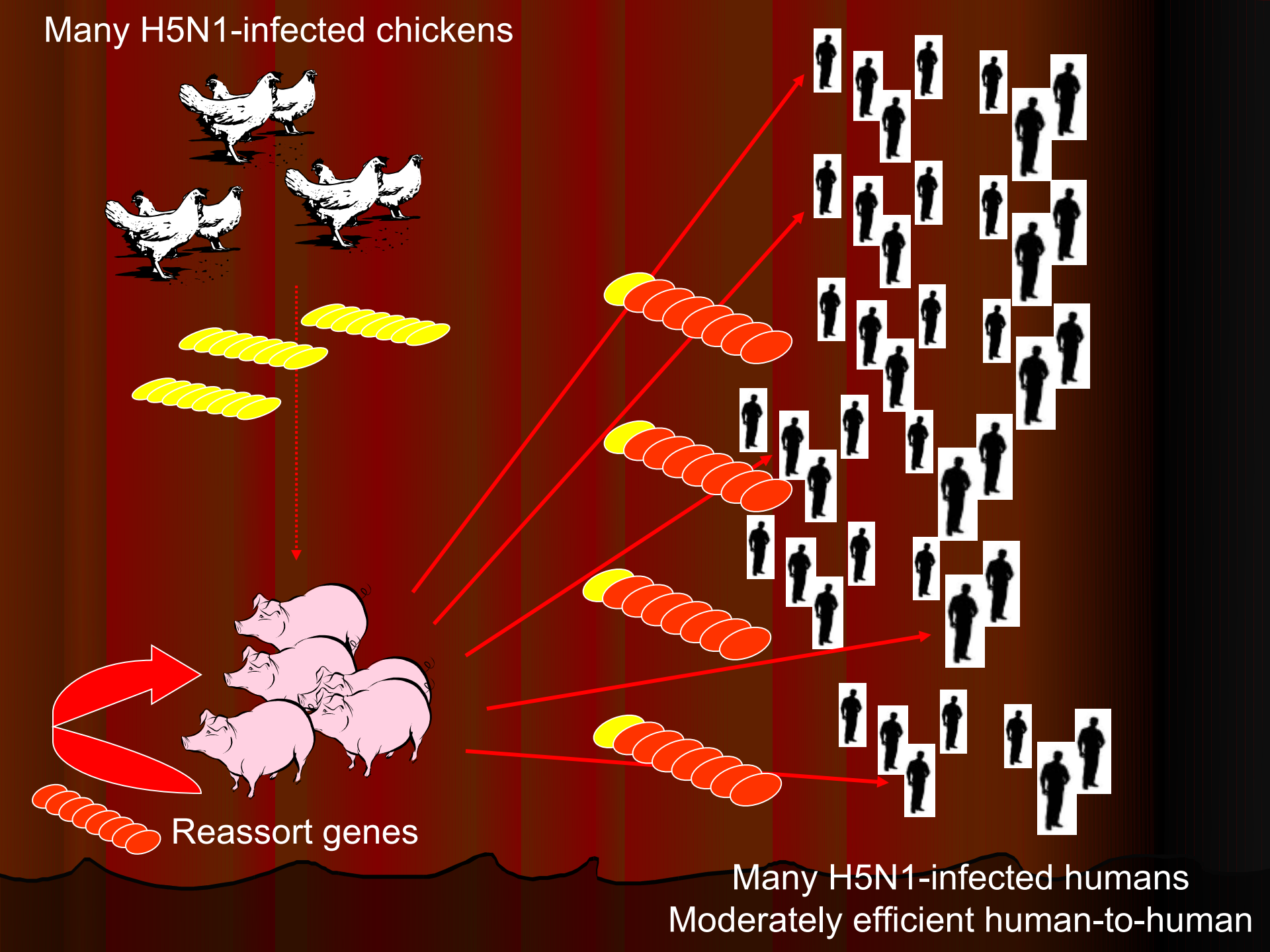
Swine flu

As of May 20th 2009



Source: WHO

http://urbangrounds.com/wp-content/uploads//swineflu.jpg


Many H5N1-infected chickens
Reassort genes
Many H5N1-infected humans
Moderately efficient human-to-human

GENETIC OF INFLUENZA A VIRUS SUBTIPE H5N1?

GENETIC CODE

A	C	D	E	F	G	H	I	K	L	M
GCU GCC GCA GCG	UGU UGC	GAU GAC	GAA GAG	UUU UUC	GGU GGC GGA GGG	CAU CAC	AUU AUC AUA	AAA AAG	UUA UUG CUU CUC CUA CUG	AUG

AMINO ACID CODE

Codon

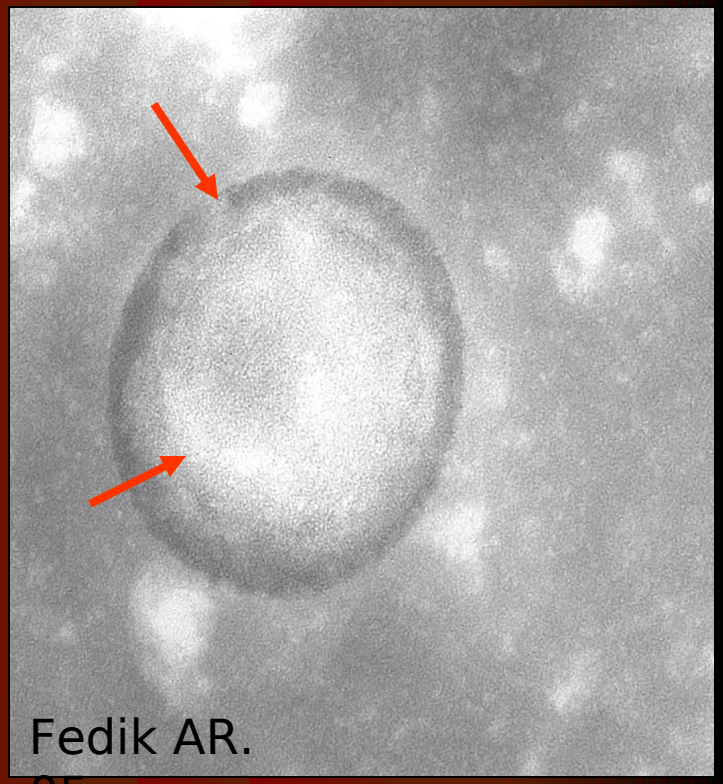
N	P	Q	R	S	T	V	W	Y	STOP
AUU AAC	CCU CCC CCA CCG	CAA CAG	CGU CGC CGA CCG AGA AGG	UCU UCC UCA UCG AGU AGC	ACU ACC ACA ACG	GUU GUC GUA GUG	UGG	UAU UAC	UAA UAG UGA

NUCLEO ACID CODE

EPITOP AND DESINFECTAN ?

Fedik AR. 05

VIRUS AI ON FECES



Fedik AR. 05

VIRUS AI AND DESINFECTANT

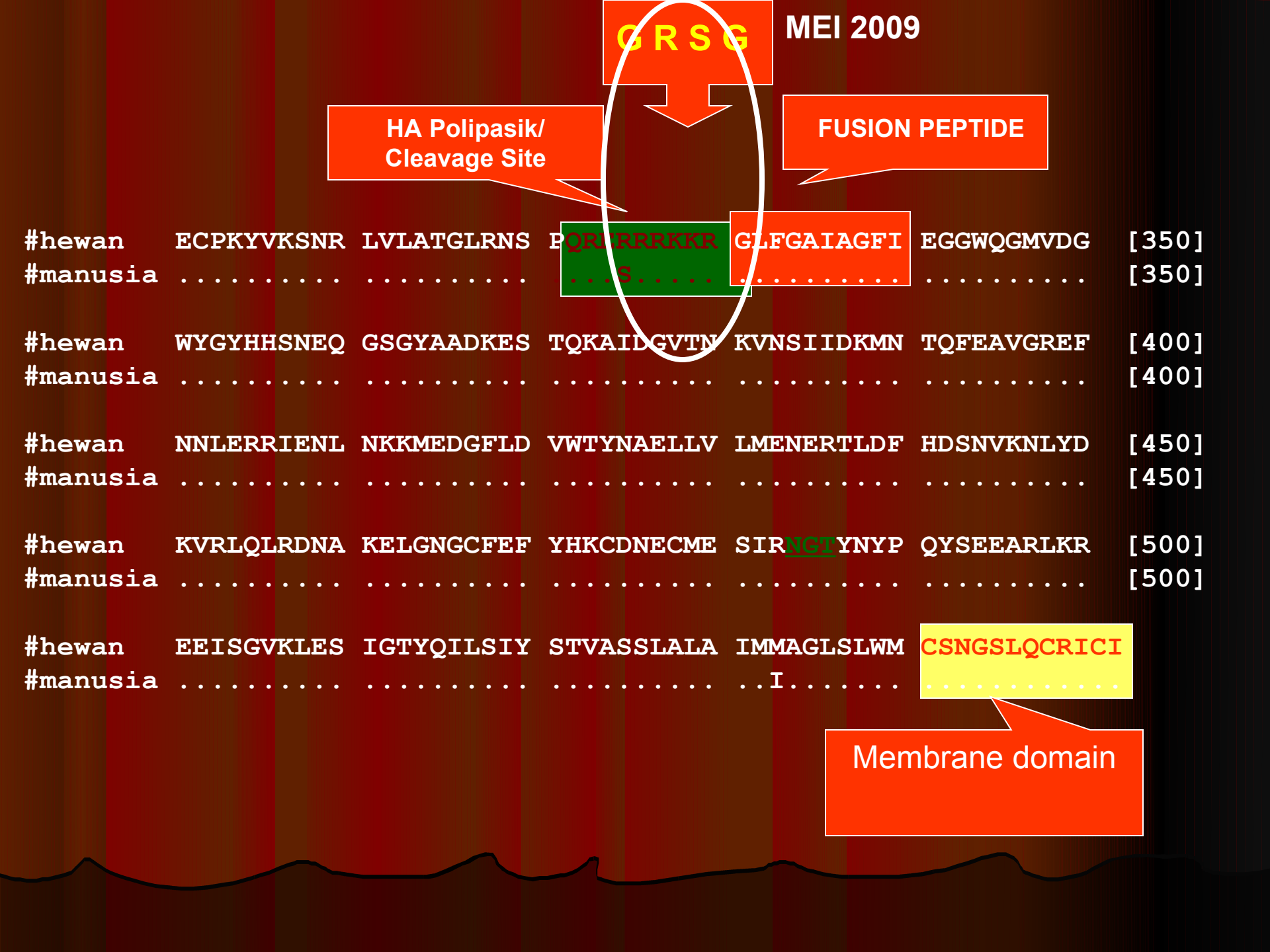
LOCALIZATION OF EPITOP PROTEIN ?

Methode	epitope residue
Cristalography analysis Ag-Ab complex	15 - 22
Sinthetic Peptida as antigenic probe	5 -8
Identification of critical residue on peptide peptide	3 - 5
Peptida squence insert into recombinan tprotein	5 - 8
Binding antipeptide antibody to protein	5 - 8
Binding antiprotein Ab modificastion protein mutation	3 - 5
Protection Ab bind residue epitope	5 - 10

GENETIC CODE

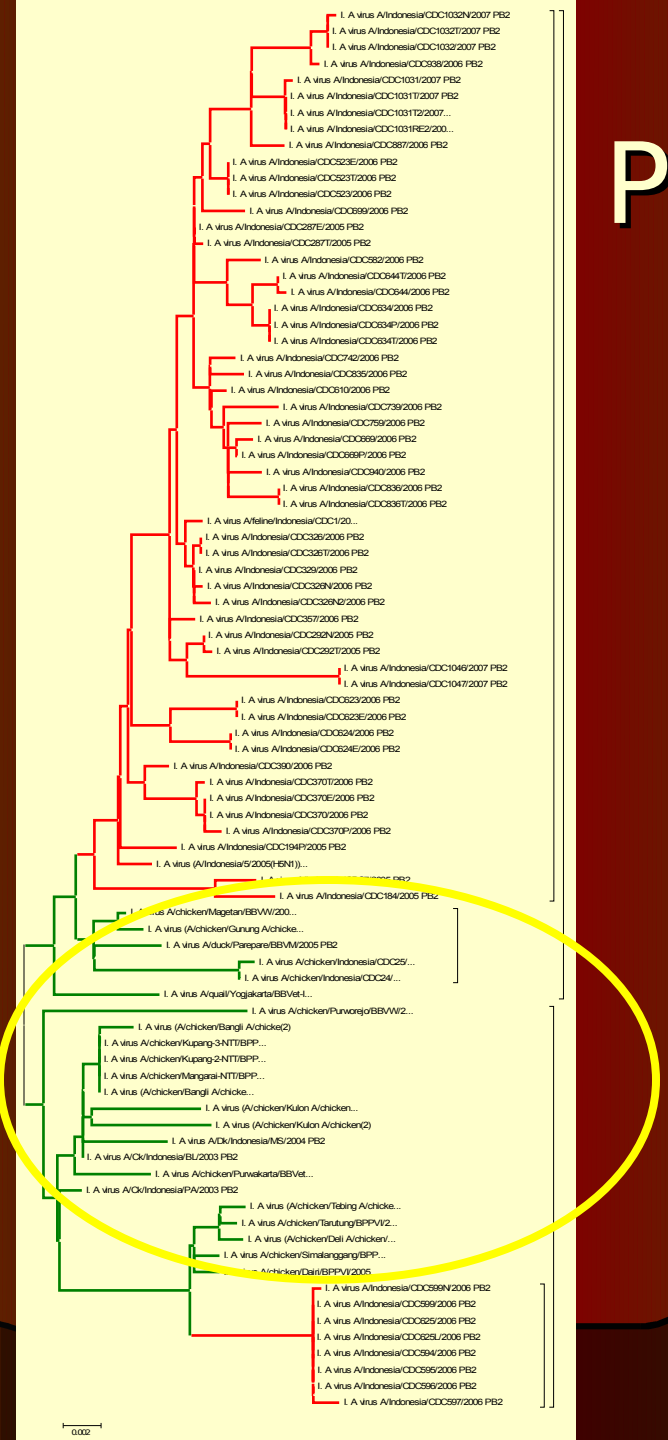
A: Alanin
B: Aspargin/aspartic acid
C: Cystein
D: Aspartic acid
E: Glutamic acid
F: Phenylalanine
G: Glycine
H: Histidine
I: Isoleucine
K: Lysine
L: Leucine

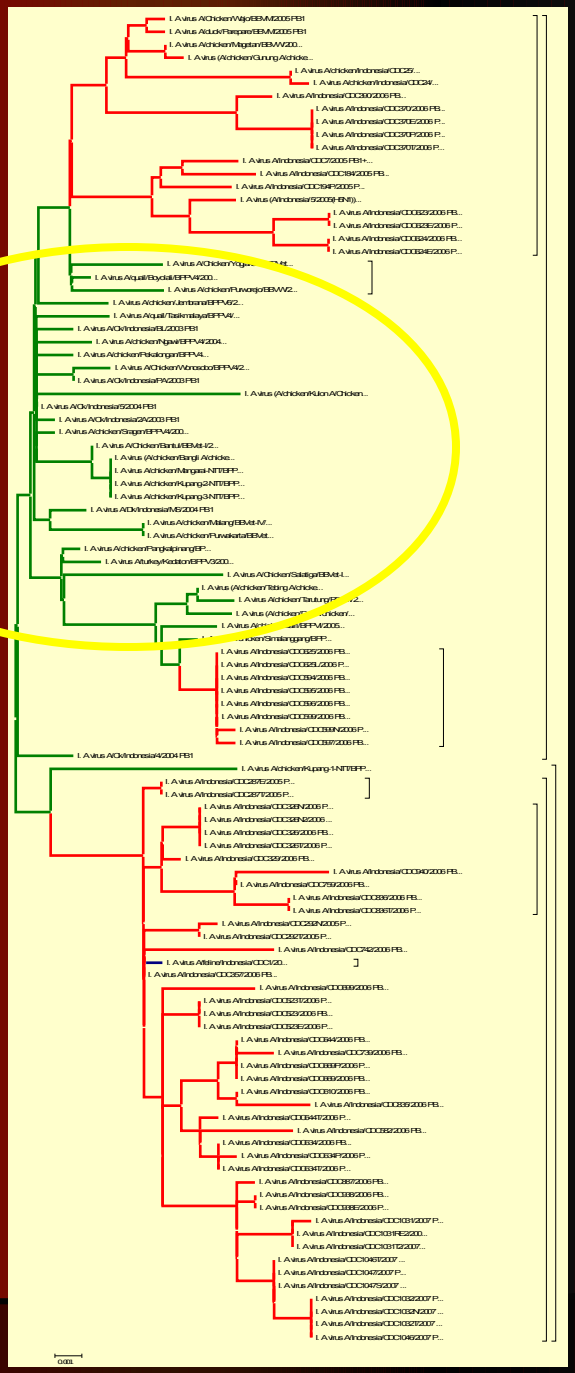
M: Methionine
N: Aspargine
P: Proline
Q: Glutamine
R: Arginine
S: Serine
T: Threonine
V: Valine
W: Tryptophane
Y: Tyrosine
Z: Glutamin/Glutamic acid


G R S G
MEI 2009
HA Polipasik/
Cleavage Site
FUSION PEPTIDE
#hewan ECPKYVKSNR LVLATGLRNS PQRERRRKKR GLFGAIAGFI EGGWQGMVDG [350]
#manusia ....S..... .... [350]
#hewan WYGYHHSNEQ GSGYAADKES TQKAIDGVTN KVNSIIDKMN TQFEAVGREF [400]
#manusia .... [400]
#hewan NNLERRIENL NKKMEDGFLD VWTYNAELLV LMENERTLDF HDSNVKNLYD [450]
#manusia .... [450]
#hewan KVRLQLRDNA KELGNGCFEF YHKCDNECME SIRNGTYNYP QYSEEARLKR [500]
#manusia .... [500]
#hewan EEISGVKLES IGTYQILSIY STVASSLALA IMMAGLSLWM CSNGSLQCRICI
#manusia ....I..... ....
Membrane domain

PB2 and PB1

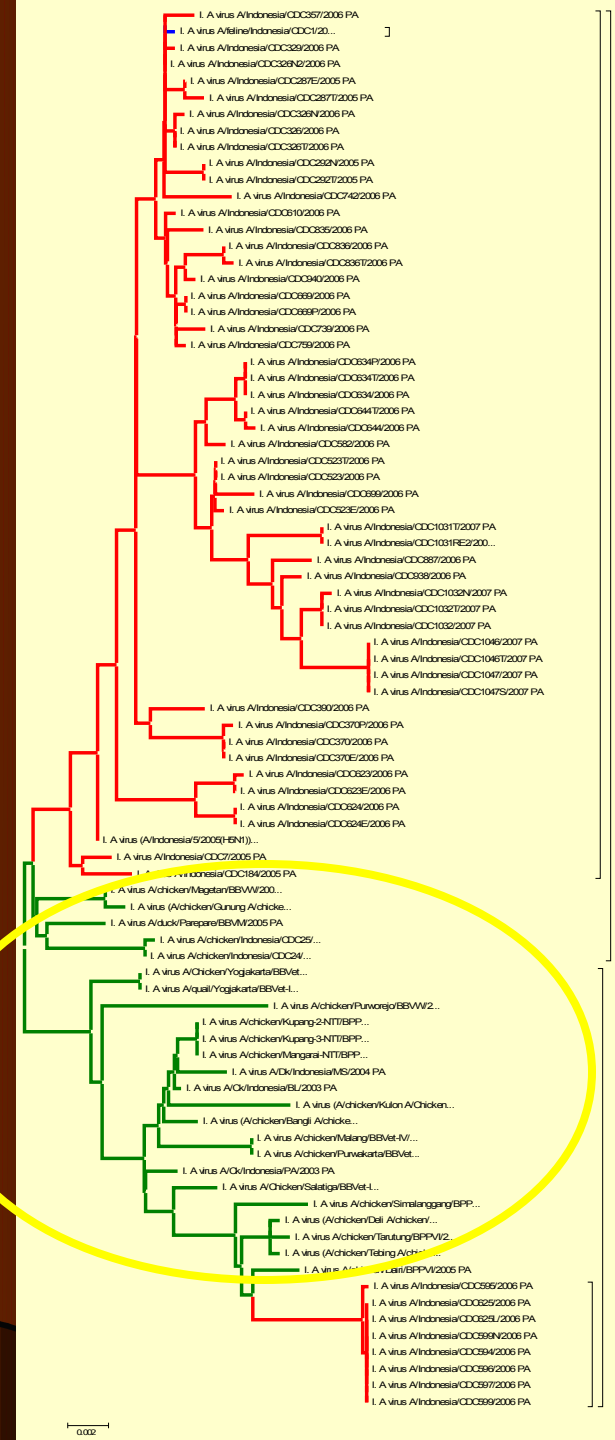
FILOGENETIK AI
ANIMAN AND HUMAN

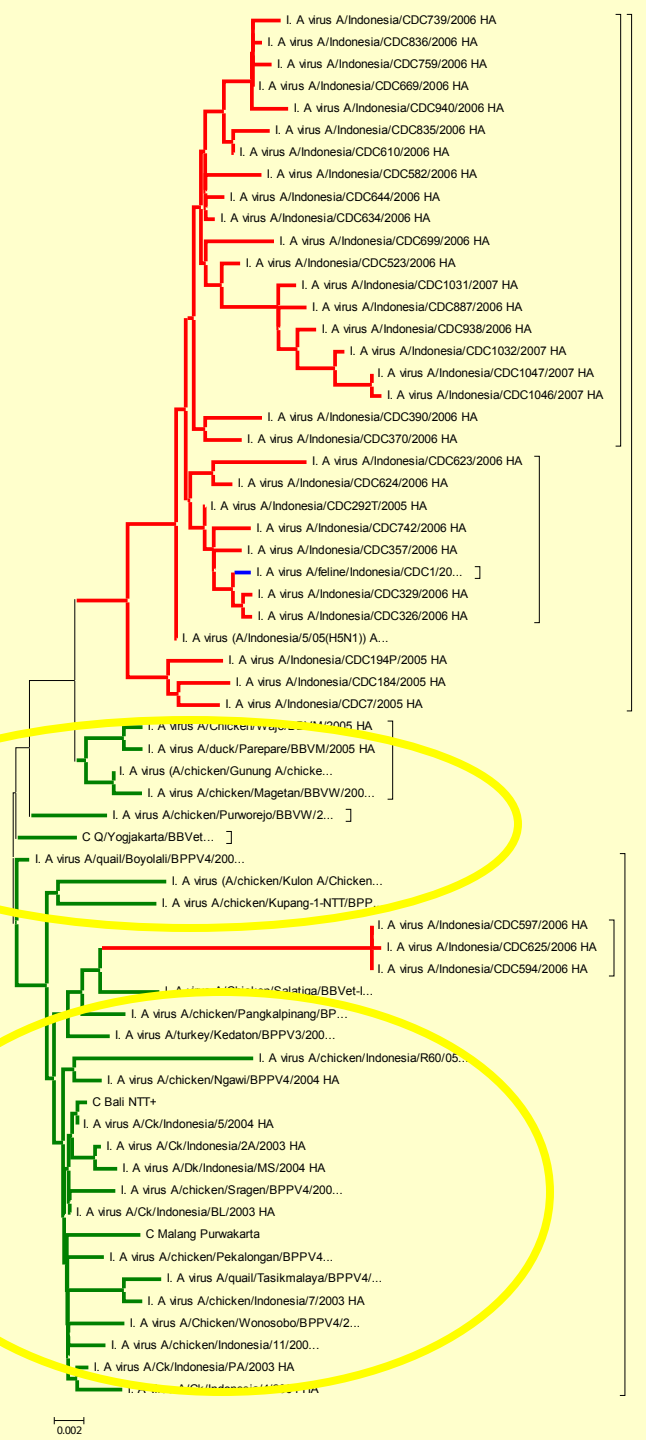




PA and HA

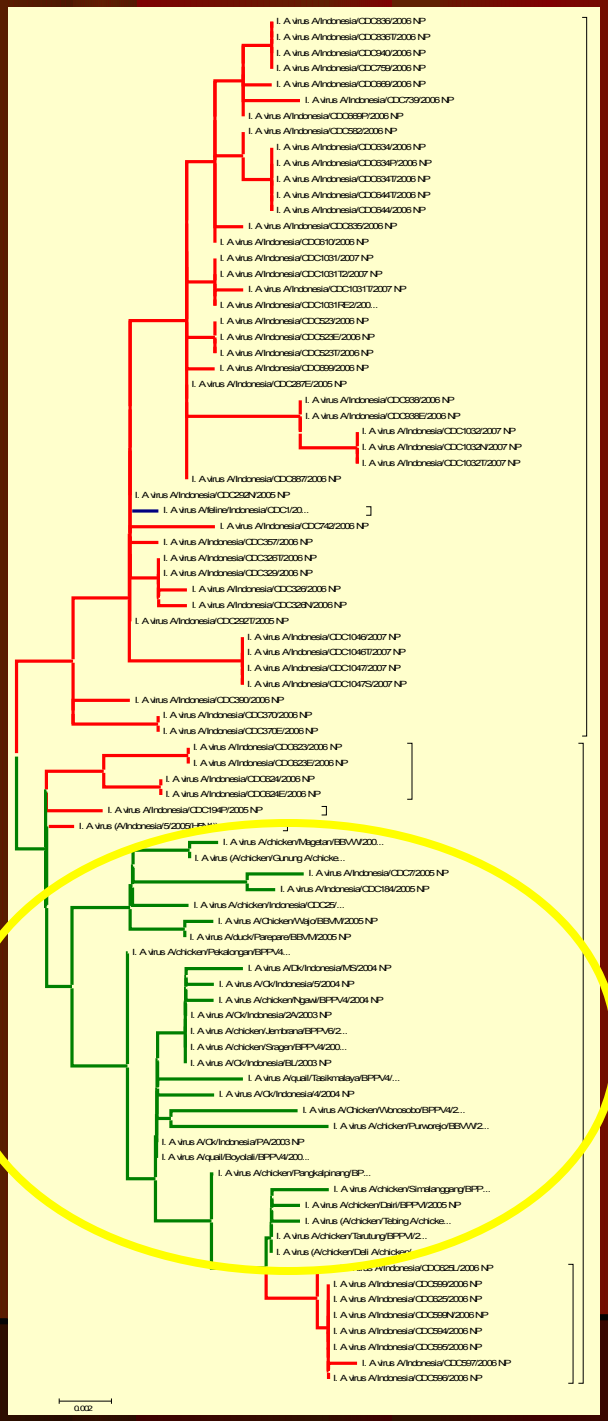
FILOGENETIK AI ANIMAN AND HUMAN

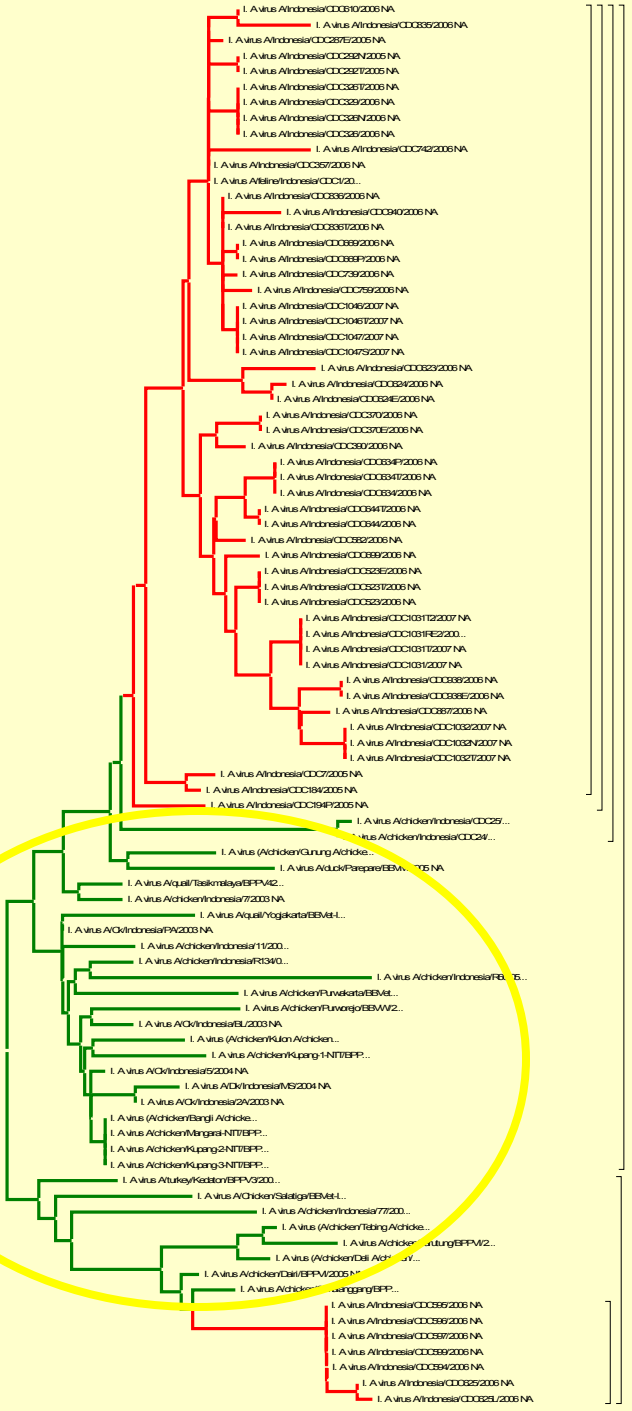


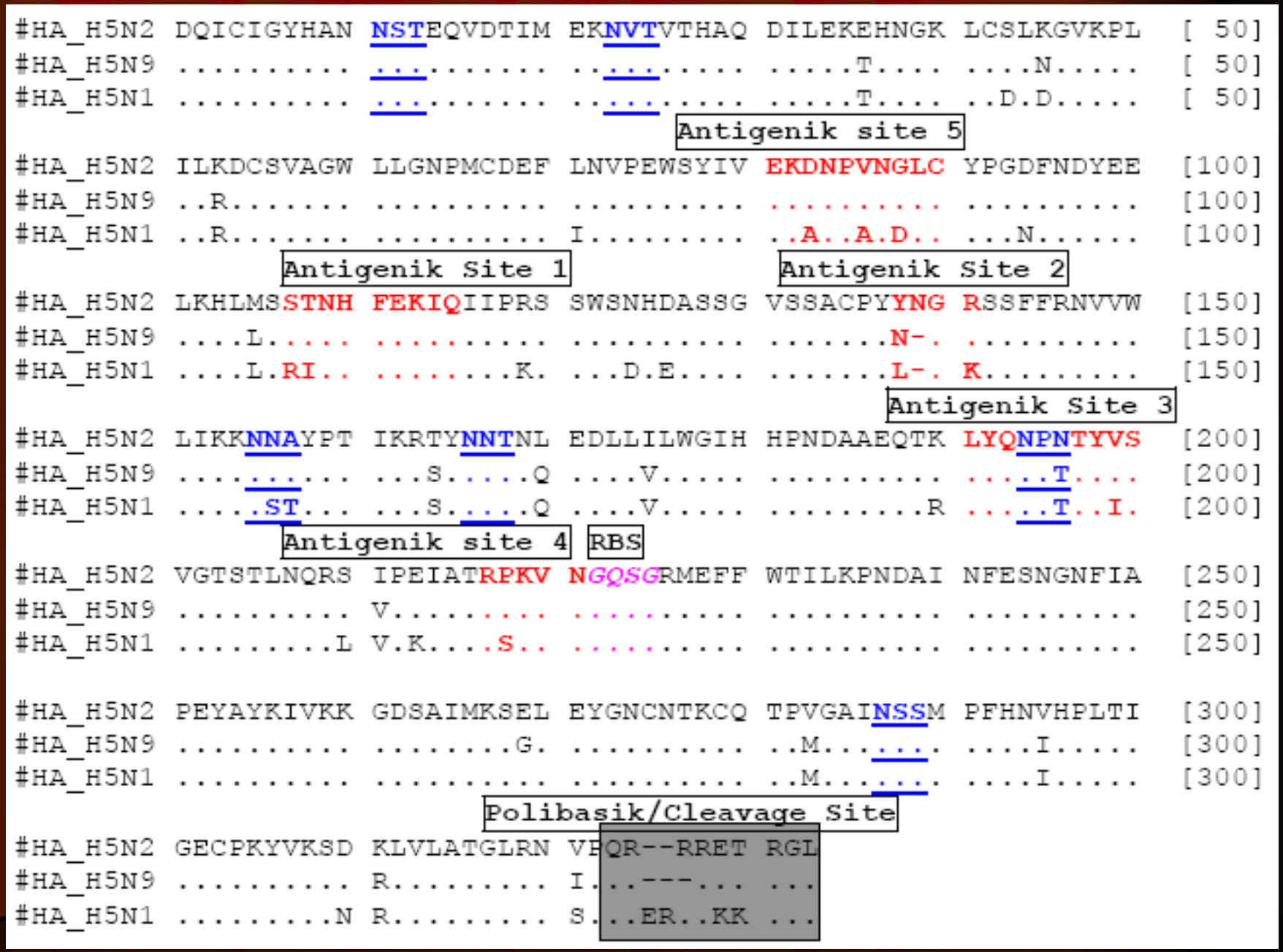


NP and NA

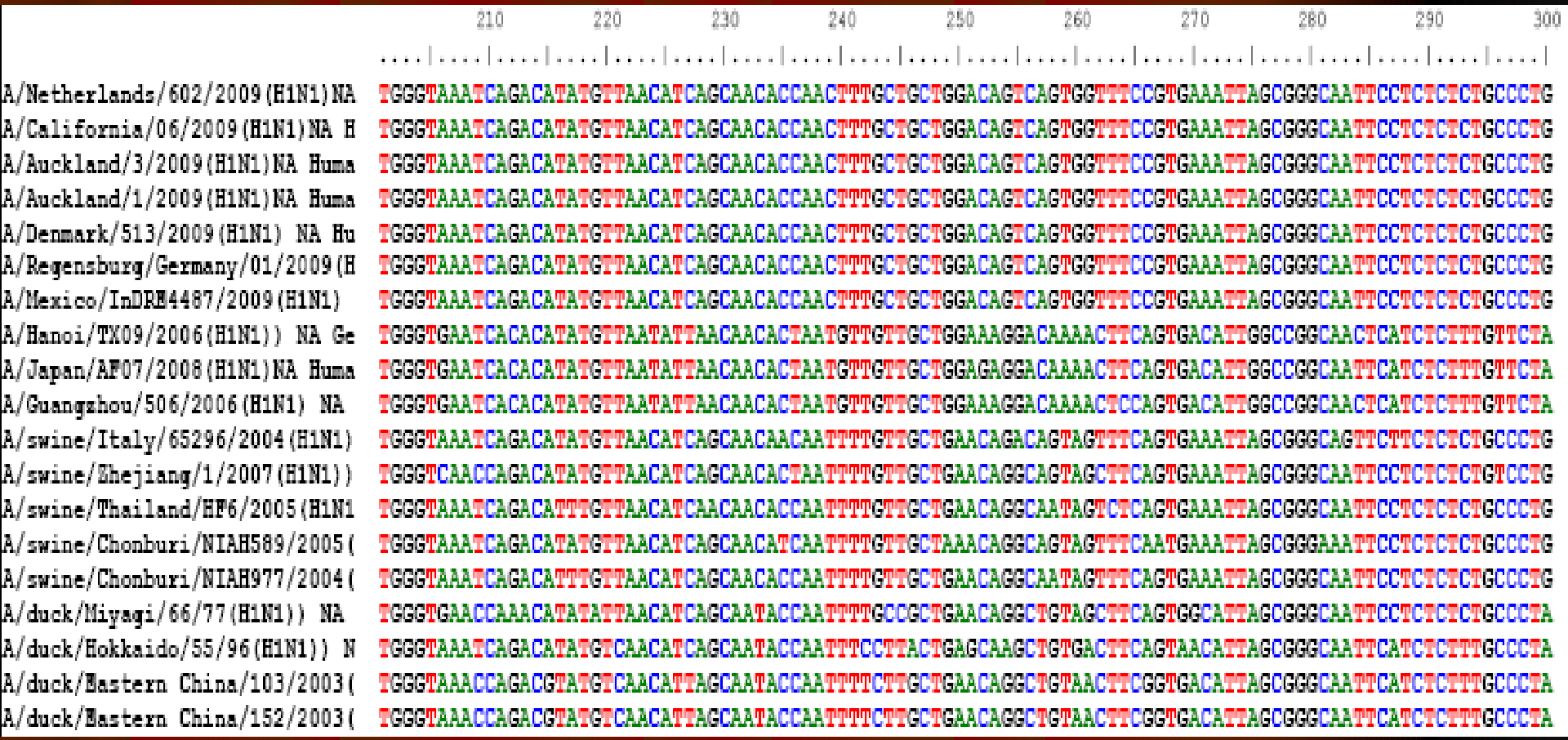
FILOGENETIK AI
ANIMAN AND HUMAN



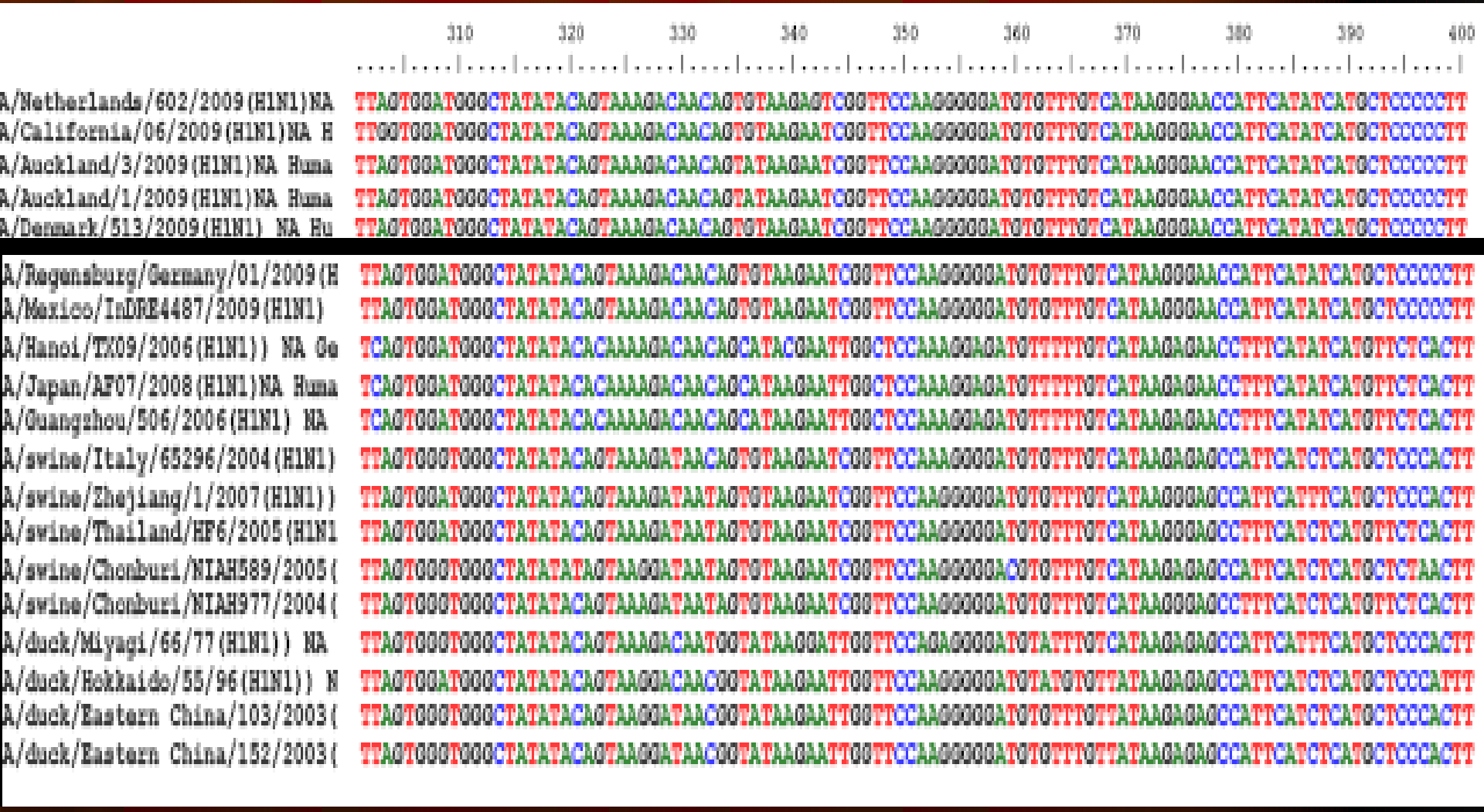



#HA_H5N2 DQICIGYHAN NSTEQVDTIM EKNVTVTHAQ DILEKEHNGK LCSLKGVKPL [50]
#HA_H5N9 ....T.... ....N..... [50]
#HA_H5N1 ....T.... ..D.D..... [50]
Antigenik site 5
#HA_H5N2 ILKDCSVAGW LLGNPMCDEF LNVPEWSYIV EKDNPVNGLC YPGDFNDYEE [100]
#HA_H5N9 ..R..... .... [100]
#HA_H5N1 ..R..... .... I......... ..A..A.D.. ...N..... [100]
Antigenik Site 1
Antigenik Site 2
#HA_H5N2 LKHLMSSTNH FEKIQIIPRS SWSNHDASSG VSSACPYYNG RSSFFRNVVW [150]
#HA_H5N9 ....L..... ....N-. .... [150]
#HA_H5N1 ....L.RI.. ....K. ...D.E.... ....L-. K......... [150]
Antigenik Site 3
#HA_H5N2 LIKKNNAYPT IKRTYNNTNL EDLLILWGIH HPNDAAEQTK LYQNPNTYVS [200]
#HA_H5N9 ....S.....Q ....V..... .....T.... [200]
#HA_H5N1 ....ST.... ...S.....Q ....V..... ....R .....T..I. [200]
Antigenik site 4
RBS
#HA_H5N2 VGTSTLNQRS IPEIATRPKV NGQSGRMEFF WTILKPNDAI NFESNGNFIA [250]
#HA_H5N9 .... V.......... .... [250]
#HA_H5N1 ....L V.K....S.. .... [250]
#HA_H5N2 PEYAYKIVKK GDSAIMKSEL EYGNCNTKCQ TPVGAINSSM PFHNVHPLTI [300]
#HA_H5N9 ....G. ..........M.....I..... [300]
#HA_H5N1 ....M.....I..... [300]
Polibasik/Cleavage Site
#HA_H5N2 GECPKYVKSD KLVLATGLRN VPQR--RRET RGL
#HA_H5N9 .... R......... I...---... ...
#HA_H5N1 ....N R......... S...ER..KK ...

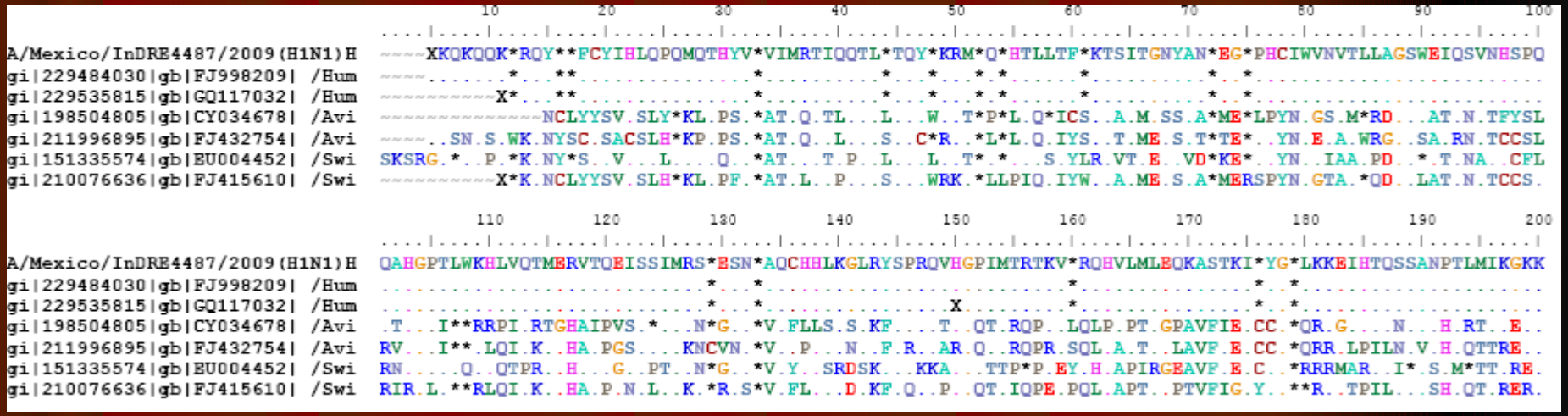
GENETICAL HOMOLOGY OF H1N1 INFLUENZA A VIRUS



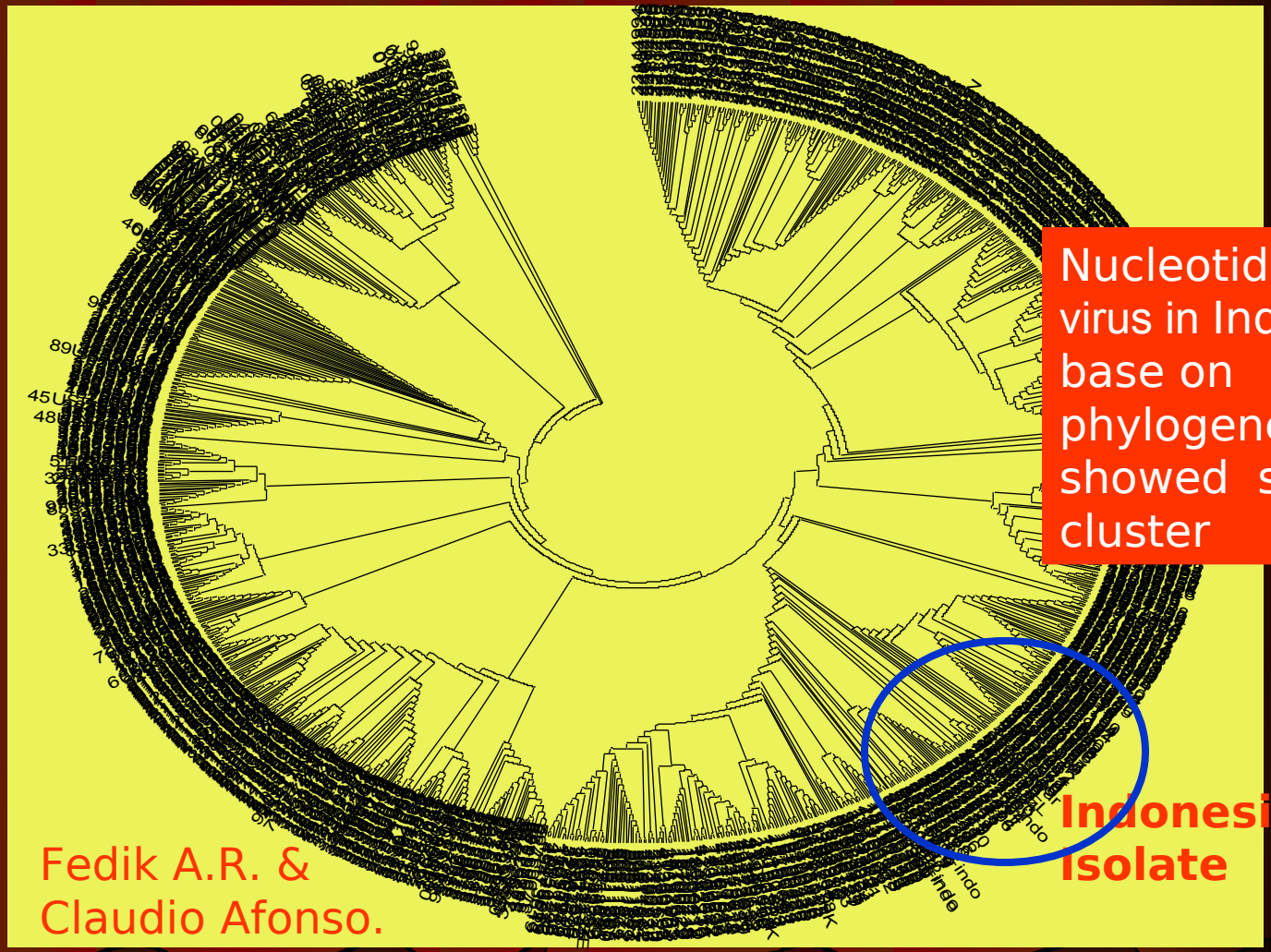
GENETICALY OF H1N1 INFLUENZA A VIRUS



GENETICALY OF H1N1 INFLUENZA A VIRUS



PHYLOGENETIC OF ND ?



PHYLOGENETIC ANALYSIS OF ND BASE ON NUCLEOTIDA IN THE WORLD

HOME WORK

1. What kinds of virus components and their function of transcription, translation and multiplication became infectious particle ?
2. What kinds of strategy of protein synthetic that are inducing of single gen ?

THANK YOU

Our future